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EXAMINER	
BERKO, RETFORD O	

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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Application Number: 10/072,320
Filing Date: February 07, 2002
Appellant(s): MUMPER ET AL.

Michael C. Barrett
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed 6/22/05 appealing from the Office action mailed 11/17/04.

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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Application Number: 10/097,232
Filing Date: March 12, 2002
Appellant(s): HEI ET AL.

Michael Barret
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed 6/22/05 appealing from the Office action mailed 11/17/04.

(1) Real Party in Interest

A statement identifying by name the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

A statement identifying the related appeals and interferences, which will directly affect or be directly affected by or have a bearing on the decision in this pending appeal is contained in the brief. The parent application is U.S. Serial No. 09/748,133 (also currently under appeal).

(3) Status of Claims

The Statement regarding the status of claims is in the brief. The statement is incorrect because claims 1-32 and 58-62 were cancelled by applicant. Claims 33-57 remained NOT claims 33-58 as alleged. When claims 48-55 were withdrawn, claims 33-47, 51 and 56-57 remained.

(4) Status of Amendments filed After Final

Applicant's statement of the status of amendments is in the brief. The statement is correct.

(5) Summary of the Invention

The summary of the invention in the brief is correct.

(6) Issues

Whether applicant's invention, a wax-film composite or bilayer film that can adhere to the skin for delivery of drug to a site is different from the invention taught in the prior art

which is a bilayer film that can adhere to a subcutaneous space and is capable of delivering drug to the site?

(7) Claims Appealed

Claims 33-58 are being appealed. The statement is incorrect because claims 1-32 and 58-62 were cancelled by applicant; thus only claims 33-57 remained. When claims 48-55 were withdrawn, claims 33-47, 51 and 56-57 remained. Therefore, claims 33-47, 51 and 56-57 remain for appeal.

(8) Prior Art of Record

US 4,959,218 Eckenhoff et al 09-1990

US 5,700,478 Biegajski et al 12-1997

On the basis of the foregoing prior art and for reasons set forth in the grounds of rejection, it is believed that the rejection should be sustained.

(9) Grounds of Rejection

The following ground(s) of rejection is applicable to the appealed claims:

Claim Rejections-35 USC Sec 103

Claims 33-47, 51, and 56-57 are rejected under 35 U.S.C. 103(a) as being unpatentable over Eckenhoff et al (US 4, 959, 218) over Biegajski et al (US 5, 700, 478).

Eckenhoff et al (Patent (218) disclosed a drug delivery device made of wax layer (col 15, lin 1-15, and lin 49) comprising layers (col 16, lin 29-39) adapted to take several forms, shapes and sizes (col 16, lin 24) made of polymers (e.g. Carbopol; col 11, lin 54) for delivering medicaments to subcutaneous spaces in an animal or human, e.g. buccal, cervical, oral sites (col 7, lin 15-25). The material used for the delivery device in Patent '2 1 8 is Carbopol also called

(Carbomer) or other water swellable polymers (col 1 1, lin 25-60) having functional groups such as hydroxyl or carboxyl groups (col 7, lin 50-60 and col 8, lin 40) as well as polyelectrolyte complexes (col 11, lin 40- 45 and lin 55-60---these functional groups and complexes render the polymer layers pH-sensitive. The layered composite delivers drug to subcutaneous, buccal, sublingual and other sites (col 7, lin 15-25, col 10, lin 30-45).

Eckenhoff et al (Patent '218) does not specifically teach the use of terms pH-sensitive, mucoadhesive; does not teach Eudragit or wt% or amounts of the ingredient polymers

Biegajski et al (Patent '478) disclosed double layered, mucoadhesive drug delivery device wherein the adhesive layer and the second polymer layer contain the drug to be delivered (abstract, col 35 lin 30). Biegajski et al disclosed the use of Eudragit polymethacrylate copolymers (col 22, lin 15) and Carbopol 934 (col 28, lin 40-45) for making the adhesive layer for the drug delivery device and the wt% of polymer components (col 8, lin 50). Biegajski et al disclosed wax-film composite wherein the mucoadhesive layer is a copolymer of methacrylic acid esters with diethylaminoethyl methacrylate (col 33, lin 55-60). Biegajski et al disclosed the melting temperature of the wax (col 9, lin 10; col 10, lin 55 and col 34, lin 35), the use of polyvinyl pyrrolidone or polyvinyl alcohol polymer (col 28, lin 40) and further disclosed that adherence of the wax-film composite to the mucosal site lasts beyond one hour (col 5, lin 25 and col 6, lin 30).

One of ordinary skill would have been motivated to make drug delivery device using polyacrylic acid cross-linked with polyalkenyl ether or divinyl glycol as the material for making the wax-film composite, giving wt% or amounts of the ingredient polymers, physical parameters such as melting point of wax, the thickness of the wax-film and the release time for the delivery

device to deliver the active substance in a time more than 1 hr as claimed by applicant. One of ordinary skill would have expected to obtain effective drug delivery of beneficial agents through the subcutaneous space over time using the method in the prior art because Biegajski et al (Patent '478) suggests the use of wax film for constructing the drug delivery device (col 4, lin 35-45 and col 5, lin 20-30) and that the thickness of the film is 5-20 mm and is shaped to fit and to conform to contoured surfaces for delivery of drug for more than 5 hours (col 7, lin 65, continue to col 8, lin 1-10). Therefore the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time it was made.

(10) Response To Arguments

1. a. Argument concerning Eckenhoff and Biegajski, alone or in combination:

Applicant argued that Eckenhof and Biegajski do not support a prima facie case for obviousness because the subject matter is different as the device in Eckenhoff et al. does not stick or adhere to the skin or mucosa surface but rather is implanted and that Eckenhoff does not teach a mucoadhesive device.

The Board should reject the argument because similar to applicant's device, Eckenhoff disclosed a delivery device made of wax layer (col 15, lin 1-15, and lin 49) comprising layers (col 16, lin 29-39) made of polymers (e.g. Carbopol; col 11, lin 54) for delivering medicaments to subcutaneous spaces in an animal or human, e.g. buccal, cervical, oral sites (col 7, lin 15-25). Carbomer is generally known in the art as an adhesive polymer and can attach to the surface of the skin. While Eckenhoff does nto use the term mucoadhesive, that term means adhere to surface of mucosa. As Eckenhoff discloses, the device delivers drug to mucosal surfaces (col 7,

lin 15-25). Even if Eckenhoff does not use the exact term "mucoadhesive", that term is used by the secondary reference (Biegajski at col 4, lin 47), which also disclosed a wax layered composite for drug delivery of drug to mucosal surface (col 9, lin 35-40, col 35, lin 49-53 and col 36, lin 5-10).

The Board should disregard applicant's argument for lack of a prima facie case for obviousness because applicant's device, similar to Eckenhoff's device touch the surface of the mucosa, are the same as both are wax-layered composites, deliver drug to the surface of the mucosa and both devices are made of the same polymer material (Carbopol or Carbomer). Carbopol is an acidic carboxy polymer, thus it is pH sensitive (col 11, lin 55-60).

1. b. Argument Concerning Biegajski

Applicant argued that the subject matter of claim 33 is different than the subject in Biegajski because the reference does not disclose, teach or suggest the pH-sensitive mucoadhesive layer of claim 33 and does not teach a wax film.

The Board should reject this argument because Biegajski was relied upon for the disclosure that a mucoadhesive layer or other polymer layers that adhere to the mucosa can be useful for affixing to mucosal surfaces for delivery of drugs (col 3, lin 27-30, lin 45-50 and col 5, lin 50-60). Applicant's invention is solving the same problem as that solved by the prior art; i.e. delivery of drug to mucosal surfaces through adhesive layers. Even if Biegajski does not use a pH sensitive polymer, the primary reference, Eckenhoff disclosed the use of polymers for drug delivery to mucosal surfaces, including the same polymers that applicant is currently claiming as his invention (Carbopol which is the same as Caarbomer; Eckenhoff, col 11, lin 55-60). Furthermore, contrary to applicant's assertions, Biegajski disclosed polymer composition with

layers, where the layer is mucoadhesive layer (Patent '478; col 4, lin 27) containing wax (Patent '478, col 4, lin 38), said delivery device is laminated and the layer is selected from waxes and fatty acid—not soluble in water (Patent 478, col 36, lin 5-9) as well as polyvinyl propylene (col 19, lin 5-10) thus suggesting water-insoluble layer. Significantly, Biegajski also contemplated other embodiments in which the adhesive film for transmucosal delivery of drug wherein the other surface of the adhesive film is covered with a substance-occlusive backing layer made of poorly soluble polymer film (col 33, lin 47-59).

2. There is suggestion or motivation to combine Eckenhoff and Bigajski

Applicant's invention is a bi-layered wax film made of water insoluble adhesive, pH sensitive polymer (e.g. Noveon or Carbomer) for delivering drug to mucosal surface, the film is less than 5 mm in thickness. The limitations in the claims specify solvents and amounts in the wax film composite.

Eckenhoff (Patent '218) disclosed delivery device that is a wax film composite (col 15, lin 12, lin 49) made of layers (col 16, lin 25-35) for delivering drugs to specific sites through the skin, the delivery device is made of polymer (Carbopol, col 11, lin 56 or Carbomer (col 14, lin 42). Thus applicant's drug delivery device is solving the same problem as the Eckenhoff's device.

Eckenhoff does not teach the words used by applicant—e.g. mucoadhesive layer, pH-sensitive and adherence. However, Eckenhoff uses the same polymeric material Carbopol or Carbomer and these are pH sensitive because they are acidic carboxy polymers (col 11, lin 55-58). Eckenhoff discussed the thickness of the film composite and the permeability or rate controlling effects through the barrier wall and indicates that it is fluid flux through a wall

forming polymeric material is most suitable when one casts the film to a thickness of 0.1 to 6 mm (col 8, lin 44-50).

Biegajski (Patent '478) was relied upon as a secondary reference because the reference, similar to Eckenhoff and applicant's invention, is in the same art, concerns drug delivery device that provides a mucoadhesive layer (col 18, lin 45-50) suitable for affixing to mucosal surface (col 4, lin 45-50), is made of wax layer (col 4, lin 35-40 and col 36, lin 5-9); and is made of polymer (col 7, lin 21-30). Significantly, Biegajski also disclosed the preferred thickness of the adhesive film to be 5-20 mm (col 7, lin 65-67) and gave examples of other thicknesses for long-term drug delivery (col 12, lin 55; col 14, lin 15-20; col 20, lin 15-20; lin 36-44 and col 23, 10-20 and lin 41-50).

The Board should sustain examiner's office action based upon obviousness theory in Graham v. Deer because Eckenhoff and Biegajske, as explained above, disclosed an invention for drug delivery wherein a wax-layered composite in the form of a film delivers drug to stites, and the thickness of the film is related to drug permeability and flux. Thus, one of ordinary skill would have been motivated to make an adhesive, polymeric drug delivery device similar to the prior art and expect to obtain effective drug delivery of beneficial agents through the subcutaneous space over time using the method in the prior art because Biegajski et al (Patent '478) suggests the use of wax film for constructing the drug delivery device (col 4, lin 35-45 and col 5, lin 20-30) and that the thickness of the film is 5-20 mm and is shaped to fit and to conform to contoured surfaces for delivery of drug for more than 5 hours (col 7, lin 65, continue to col 8, lin 1-10). Therefore the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time it was made.

For the limitations in the dependent claims presented and evaluated in the final office action, currently under appeal, examiner identified the limitations as follows:

For Claim 34; Eckenhoff (Patent '218) discloses the use of 100 g of wax in the layer (co l 15, lin 1). Biegajski (Patent '478) also disclosed waxes in the composite layer (col 36, lin 5-50).

For claim 35; Patent '218 discloses Carbopol, same as Carbomer but only with different trademark, as acidic carboxy polymer (col 11, lin 56) showing amounts of 670g/700 ml at col 14, lin 42). According to Patent '218, Carbomer disclosed is the sodium salt of polyacrylic acid (col '218, lin 42-43). In addition, Biegajski (Patent '478) also disclosed the use of Carbopol polymer (col 7, lin 28).

For claim 36, Patent '218 disclosed swellable polymer polyacrylic acid (col 11, lin 61) cross-linked with polyhydroxyalkylmethyacrylate or polyvinylpyrrolidone (col 11, lin 43 and lin 38).

For claim 37, Patent '218 disclosed the use of Carbomer (a synthetic polymer, whose different tradename is Carbopol)

For claim 38, is amount of Carbopol or Carbomer a ; discussed above in claim 35.

For claim 39, Patent '218 disclosed copolymer of methacrylic acid derivative (col 11, lin 38-45).

For claim40, limitation is amount of pH sensitive polymer, similar to claims 35 and 38).

For claim 41, Patent '478 disclosed the use of Eudragit polymer rather than Carbomer or Carbopol (col 22, lin 16-20). Eudragit S100 is a methacrylic copolymer. Patent '478 also disclosed copolymers of methacrylic acid (col 33, lin 55-60).

For claim 42, Patent '218 disclosed a water-swellable polymer (col 11, lin 33-39). The melting point that is claimed is a physical property of the polymer and the limitation is met when applicant uses the same polymer disclosed in the prior art. In this respect, Patent '478 disclosed hydrophobic polymer material that will not dissolve at below 40 degrees (col 10, lin 53-54).

For claim 43, Patent '218 does not identify a specific wax, but Patent '478 disclosed paraffin wax (col 4, lin 39).

For claim 44 Patent '218 disclosed 100g wax in the layer (col 15, lin 1-5) but Patent '478 did not disclose any amounts.

For claim 45, is the same limitation as claim 36. Patent '218 Patent '218 disclosed swellable polymer polyacrylic acid (col 11, lin 61) cross-linked with polyhydroxyalkylmethyacrylate or polyvinylpyrrolidone (col 11, lin 43 and lin 38).
For claim 46, the limitation is a wax layer. Patent '218 discloses the use of 100 g of wax in the layer (col 15, lin 1).

For claim 47, Patent '218 disclosed that the drug delivery device; a wax-film composite, delivers drug (e.g. peptide hormone, col 15, lin 43 and col 10, lin 30-45). Significantly, Patent '478 disclosed delivery of drugs including anesthetic, sweetner, analgesic and flavoring agents (col 36, lin 30-65).

Claims 48-55 were not considered in the final office action as the claims were withdrawn by applicant. Also applicant cancelled claims 58-62.

For claim 56, Patent 'disclosed that the delivery device is adapted to deliver beneficial agents to anorectal, buccal, oral, cervical sublingual sites (col 7, lin 15-25).

For claim 57, the limitation requires adherence of the delivery device to the site of application. Though Patent '218 does not specifically use the term adherence or attachment, an embodiment contemplated by the invention is adapted for implantation (col 3, lin 47, col7, lin 15). Implantation includes attachment, therefore Biegajski (Patent 478) was relied upon as disclosing a drug delivery device that is affixed to mucosal surface (col 3, lin 45-50, col 5, lin 10; col 14, lin 45-50 and col 24, lin 29) adheres to the mucosal surface because it an adhesive layer (col 6, lin 58).

Conclusion

The Board should reject applicant's arguments because examiner has shown that applicant's invention is not patentable as the invention would have been obvious to one of ordinary skill in the art on the theory of Graham v. Deer given the disclosures in Eckenhoff and Biegajski.

The invention is directed toward a drug delivery device that can attach to mucosal surface, made of polymeric, mucoadhesive material with specified thickness for drug delivery. Both Eckenhoff and Biegajski disclosed drug delivery devices in the same field of art, disclose wax-layered architecture with thickness. Because Biegajske disclosed several thicknesses of the delivery device, e.g. 5 mm (col 7, lin 61), 35 mm (col 12, lin 55) 5 mm (col 14, lin 16); 35 mm (col 15, lin 66)30 mm (col 20, lin 31 and 5 mm (col 23, lin 40-45); and the thickness reduces the amount of drug that is delivered to the site (col 25, lin 25-30) or the penetration rate (col 14, lin 15-20); one of ordinary skill can without undue experimentation determine the uptimum Ron thickness of the composite for the best delivery of drug.

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